REMARKS

Claims 15 through 27 are under examination in this application.

Applicant's representative, Scott Rothenberger, spoke with Examiner Fay on September 20, 2007 in order to clarify the pending rejections. It was noted that Claims 1-14 were rejected under 35 U.S.C. § 102(b). Claims 1-14 are not pending. It was also noted that it was not clear if the rejection pertained to claims 15-27. Examiner Fay requested that the response address claims 15-27. Additionally, claims 1-28 were rejected under 35 U.S.C. § 112, first paragraph. Only claims 15-27 are pending. There is no claim 28 pending.

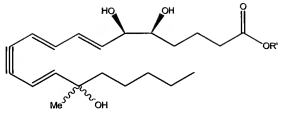
Examiner Fay stated that Applicant should respond to the rejections in view of the pending claims and that another **subsequent non-final office action** would be issued if necessary after review of this response.

Applicant's representative agreed to respond in the view of the comments above and in view of a further non-final office action if required.

Rejection of Claims 15-27 under 35 U.S.C. § 102(b)

Claims 15 through 27 stand rejected under 35 U.S.C. § 102(b) as being anticipated by WO 90/13292, hereinafter "'292". Applicant respectfully traverses this rejection for at least the following reasons.

The present invention pertains to a method for treating columnar epithelial inflammation in a subject comprising, administering to a subject an effective amount of a lipoxin A_4 compound, wherein the lipoxin compound is an analog of natural lipoxin A_4, and wherein the **analog of natural lipoxin A_4 has a longer half-life than natural lipoxin A_4**. For example, on such lipoxin compound has the formula



where R' is H or CH_3.

The '292 publication provides ONLY for lipoxin A_4. The '292 also discloses "analogues" of lipoxin A_4 but does not provide any guidance what such analogues could be.

The '292 publication fails to teach or suggest ANY analogue let alone an lipoxin compound that is **analog of natural lipoxin A_4 that has a longer half-life than natural lipoxin A_4**.

Moreover, the category of lipoxins is a broad genus and "[t]o establish a prima facie case of obviousness in a genus-species chemical composition situation...some motivation or suggestion to make the claimed invention in light of the prior art teachings" must be identified. MPEP 2108.08

Although this is not an obviousness type rejection, the basic argument is still applicable. There is simply no teaching of any specific (species) analogs of lipoxin A_4 in the '292 publication.

Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claims 15-27 Under 35 U.S.C. § 112, First Paragraph

Claims 15 through 27 were rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for treating certain disorders associated with columnar epithelial inflammation, does not reasonably provide enablement for treating all conditions associated with columnar epithelial inflammation. Applicant respectfully traverses the rejection for at least the following reason.

The following arguments presented below refer to paragraph number notations from Applicant's published patent application US 2004/0151712 A1.

Example 4 of the specification discusses activity of lipoxin analogs on columnar epithelia.

Activity of Lipoxin Analogs on Columnar Epithelia

[0184] Several of the preferred lipoxin analogs (shown structurally as compounds 1 through 8 in Example 3) were prepared by total synthesis as described in Example 2. Following preparation and isolation of these compounds via HPLC, compounds were assessed to determine whether they retain biological activity using the epithelial cell transmigration assays as described above in Example 1.

[0185] Compounds 1 through 8 (10^{-7}-10^{-10}M) were found to inhibit neutrophil transmigration on epithelial cells. The acetylenic precursors (compound 1, 3, 5 and 7) were found to be physically more stable than their tetraene counterparts. Compound 7, which did not have an alcohol group in the C15 position or other modifications in the series, showed no biological activity in the assays. It would therefore appear that a substituent in the C15 position of lipoxin is necessary for the biological activity of at least lipoxin A_4 analogs. Lipoxin analogs 1 through 8 were found to block migration at potencies greater than or equal to synthetic lipoxin A_4. Compounds 1, 2 and 4 were found to be particularly effective. The results indicate that lipoxin A_4 analogs with modifications in C15-C20 positions retain their biological action and can inhibit PMN transmigration in columnar epithelia.

PMN transmigration is associated with inflammation.

Inflammation of the columnar epithelia is associated with various disease conditions.

[0017] Epithelial perturbations cause or contribute to inflammatory intestinal disease states including: acute self-limited enterocolitis; viral infections such as non-specific enteritis or specific viral enteritis; ulcerative colitis; Crohn's disease; diverticulitis; bacterial enterocolitis, such as salmonellosis, shigellosis, campylobacter enterocolitis, or yersinia enterocolitis; protozoan infections such as amebiasis; helminthic infection; and pseudomembraneous colitis.

[0018] Additional inflammatory intestinal diseases are duodenitis resulting caused by infections, physical and chemical injuries, Celiac disease, allergic disease, immune disorders or stress ulcers; lymphocytic colitis; collagenous colitis; diversion-related colitis; acute self-limited colitis; microscopic colitis; solitary rectal ulcer syndrome; Behcet's disease; nonspecific ulcers of the colon; secondary ulcers of the colon; ischemic bowel disease; vasculitis; peptic duodenitis; peptic ulcer; bypass enteritis; ulcerative jejunoileitis; or nonspecific ulcers of the small intestine. Malabsorptive disorders include mucosal lesions associated with altered immune response such as idiopathic AIDS enteropathy, with viral or bacterial infections, or with miscellaneous diseases such as mastocytosis or eosinophilic gastroenteritis.

[0019] Perturbations of the epithelia of the lung and trachea cause or contribute to inflammatory lung diseases such as: cystic fibrosis, bronchiolitis, bronchitis, asthma, interstitial lung disease, eosinophilic pneumonias, tracheobronchitis, tracheoesophageal fistulas, and alveolitis.

[0020] Perturbations of the epithelium of the kidney cause or contribute to diseases such as: glomerulonephritis, nephritis, polycystic disease, ischemic disease, immune-complex-induced disease, immunopathogenic injuries, pyelonephritis, and tubulointerstitial disease.

[0021] Perturbations of the epithelium of the stomach cause or contribute to diseases such as gastritis and stomach ulcers.

[0022] This invention also encompasses inflammation of columnar epithelial caused or contributed to by surgery, allergy, chemical exposure, and physical injury.

The Office Action alleges that the specification is not enabled for the method of treating any epithelial inflammation since there are numerous inflammation diseases and the specification does not teach how to treat all of the possible variations of inflammation.

Applicants submit as Exhibit A ,pages from an immunology textbook (Kuby, Immunology, New York: W.H. Freeman and Company, 1992), which describes the inflammatory response in general terms both textually and graphically on page 8, and provides more detailed description on pages 264-266. These descriptions lack any suggestion that the

inflammatory response varies from tissue to tissue or from condition to condition, as suggested by the present Office Action.

MPEP 2107.03 provides that :"The Office must confine its review of patent applications to the statutory requirements of the patent law. ... Thus, while an applicant may on occasion need to provide evidence to show that an invention will work as claimed, it is improper for Office personnel to request evidence of safety in the treatment of humans, or regarding the degree of effectiveness." (citations omitted)) Factual support for the positions taken in the Office Action is largely absent, yet such support is required to sustain an enablement rejection (MPEP 2164.04: "'it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.'" (quoting *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971)).

The Federal Circuit recently articulated a standard whereby the PTO must establish a rational connection between the agency's fact-findings and its ultimate action. *Dickinson v. Zurko*, 119 S.Ct. 1816 (1999). In light of Applicants' arguments of record, and the presumption in favor of Applicants, it is respectfully asserted that the present rejection is not supported by substantial evidence, and as such, fails to rise above the "arbitrary, capricious" standard applied under the "substantial evidence" test of Section 706(2)(E) of the Administrative Procedure Act. The Office Action has not cited any relevant art nor relied on any other fact-finding results to rebut the presumption in favor of Applicants. If the Examiner is relying on personal knowledge, Applicants respectfully request that the Examiner provide an affidavit pursuant to 37 C.F.R. 1.104(d)(2). In view of the above arguments and reasoning, Applicants respectfully request reconsideration and withdrawal of this rejection.

In summary, the specification enables one skilled in the art to treat columnar epithelial inflammation.

Reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

In light of the above, it is respectfully submitted that the present application is in condition for allowance. Reconsideration of the present application and a favorable response are respectfully requested. If a telephone conference would be helpful in resolving any remaining issues, please contact the undersigned at 612-340-8819.

No additional claim fees should be generated by this paper. However, the Commissioner is hereby authorized to charge any deficiencies or credit any overpayments to Deposit Account No. 04-1420.

Respectfully submitted,

DORSEY & WHITNEY LLP

Customer Number 25763

Date: September 24, 2007

By: _____

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